WHAT IS CLAIMED IS:

1. A method for identifying the nucleotide at one or more base positions in a target nucleic acid molecule, comprising:

synthesizing extension products of the target nucleic acid in the presence of chain terminating nucleotides and mass-matched nucleotides;

determining the mass of each extension product; and

calculating a mass shift from a period for the mass of each extension product,

whereby nucleotide(s) at one or more base positions is determined by identifying the nucleotide that corresponds to each mass shift.

2. The method of claim 1 that is a method for determining a nucleotide sequence of a target nucleic acid, comprising:

synthesizing extension products of the target nucleic acid in the presence of chain terminating nucleotides and mass-matched nucleotides;

determining the mass of each extension product; and

calculating a mass shift from a period for the mass of each extension product,

whereby the nucleotide sequence of the target nucleic acid is determined by assigning a nucleotide corresponding to each mass shift.

3. The method of claim 1, wherein the mass-matched deoxynucleotides are identical.

4. The method of claim 1, wherein a mass-matched deoxynucleotide is deoxyinosine, 5-nitroindole, 3-nitropyrrole , 3-methyl 7-propynyl isocarbostyril, 5-methyl iscarbostyril or 3-methyl iscarbostyril.

5. A method for identifying nucleotides at one or more base positions in a plurality of target nucleic acids molecules, comprising:

synthesizing extension products of the target nucleic acid in the presence of chain terminating nucleotides and mass-matched nucleotides;

determining the mass of each extension product; and

calculating a mass shift from a period for the mass of each extension product,

whereby the nucleotides in the target nucleic acid molecules are identified by determining the nucleotide that corresponds to each mass shift.

6. The method of claim 5 that is a method for determining nucleotide sequences of a plurality of target nucleic acids molecules, comprising:

synthesizing extension products of the target nucleic acid in the presence of chain terminating nucleotides and mass-matched nucleotides;

determining the mass of each extension product; and

calculating a mass shift from a period for the mass of each extension product,

whereby the nucleotide sequences of the target nucleic acids are determined by determining the nucleotide that corresponds to each mass shift.

7. The method of claim 5, wherein the mass-matched deoxynucleotides are identical to one another.

8. The method of claim 1, wherein a mass-matched deoxynucleotide is deoxyinosine, 5-nitroindole, 3-nitropyrrole , 3-methyl 7-propynyl isocarbostyril, 5-methyl iscarbostyril or 3-methyl iscarbostyril.

9. A method for identifying nucleotides at one or more base positions in a plurality of target nucleic acids molecules, comprising:

synthesizing extension products of the target nucleic acid in the presence of chain terminating nucleotides and mass-matched nucleotides;

determining the mass of each extension product; and

calculating a mass shift from a period for the mass of each extension product,

whereby the nucleotides in the target nucleic acid molecules are identified by determining the nucleotide that corresponds to each mass shift.

10. A method for determining a nucleotide sequence of a target nucleic acid molecule, comprising:

incorporating pair-matched nucleotides into the target nucleic acid;

synthesizing extension products of the target nucleic acid in the presence of a partially duplex hairpin primer, chain terminating nucleotides and pair-matched nucleotides;

determining the mass of each extension product; and

calculating a mass shift from a period for the mass of each extension product;

whereby the nucleotide sequence of the target nucleic acid is determined by assigning a nucleotide corresponding to each mass shift.

11. The method of claim 10, wherein the chain terminating nucleotides are mass-matched.

12. The method of claim 10, wherein the chain terminating nucleotide base pairs have distinct molecular weights.

13. A method for determining nucleotide sequences of a plurality of target nucleic acids, comprising:

incorporating pair-matched nucleotides into the target nucleic acids;

synthesizing extension products of the target nucleic acids in the presence of a partially duplex hairpin primer, chain terminating nucleotides and pair-matched nucleotides;

amplifying the target nucleic acid sequences in the presence of pair-matched nucleotides;

determining the mass of each extension product; and

calculating a mass shift from a period for the mass of each extension product;

whereby the nucleotide sequences of the target nucleic acids are determined by assigning a nucleotide corresponding to each mass shift.

14. The method of claim 13, wherein the chain terminating nucleotides are mass-matched.

15. The method of claim 13, wherein the chain terminating nucleotide base pairs have distinct molecular weights.

16. The method of claim 13, wherein the primers are mass-labeled.

17. A method for detecting a one or a plurality of target nucleic acid(s) or one or plurality of nucleotides therein molecules, comprising:

(a) copying the target nucleic acid molecule(s) in the presence of a pair-matched set of nucleotides;

(b) denaturing the resulting copies of the target(s) to produce single-stranded templates;

(c) annealing and ligating one or a plurality of partially duplex hairpin primers to the single-stranded template(s);

(d) extending the primer(s) in the presence of chain terminating nucleotides and pair-matched nucleotides to produce extension products, wherein the extension products follow a periodic mass distribution that is determined by the mass of the pair-matched nucleotide set; and

(e) detecting each of the targets or nucleotides therein the by virtue of rom the mass shift of each extension product from its corresponding periodic reference mass.

18. The method of claim 17, wherein the chain terminating nucleotides are mass-matched.

19. The method of claim 17, wherein the chain terminating nucleotide base pairs have distinct molecular weights.

20. The method of claim 17, wherein the primers are mass-labeled.

21. A kit for determining the sequence of a target nucleic acid, comprising mass-matched nucleotides.

22. A kit for determining the sequence of a target nucleic acid, comprising pair-matched nucleotides and mass-matched chain terminating nucleotides.

23. A kit for determining the sequence of a target nucleic acid, comprising pair-matched nucleotides and chain terminating nucleotides that form base pairs of distinct molecular weight, and optionally including instructions for sequencing using these reagents.

24. A kit for determining the sequence of a target nucleic acid, comprising pair-matched nucleotides and mass-labeled primers, and optionally including instructions for sequencing using these reagents

25. A method for detecting different nucleotide base compositions in a population of nucleic acids having identical length, comprising:

synthesizing the nucleic acids in the presence of one or more nucleotide analogs to produce synthesized nucleic acids; and

determining a mass of each synthesized nucleic acid;

whereby different nucleotide base compositions are detected by determining the mass of each synthesized nucleic acid,

wherein the nucleotide analog separates the masses of nucleic acids having different base compositions in a predetermined interval.

26. The method of claim 25, wherein the population of nucleic acids having identical length and different base compositions differ in base composition by a single base.

27. A method for detecting a plurality of target nucleic acid molecules in a sample containing nucleic acid molecules, comprising:

preparing a composition containing plurality of pair-matched nucleic acid molecules or mass-matched nucleic acid molecules from a sample comprising the target nucleic acid molecules;

analyzing the resulting composition by mass spectrometry; and

detecting target nucleic acid molecules.

28. A process for detecting a mutation in a target nucleic acid sequence in a target nucleic acid molecule, in a sample, comprising:

a) hybridizing a nucleic acid molecule a primer to nucleic acid molecules in the sample, thereby producing a hybridized primer and a molecule from the sample, wherein:

the nucleic molecules from the sample are optionally immobilized;

the primer is complementary to a sequence in the target nucleic acid sequence that is adjacent to the region suspected of containing a mutation sequence;

b) contacting the hybridized primer with a composition comprising mass-matched deoxyribonucleoside triphosphates and a chain terminating nucleotide selected from a dideoxyribonucleoside triphosphate or a 3'-deoxynucleoside triphosphate and optionally one or more deoxyribonucleoside triphosphates, such that the hybridized primer is extended until a chain terminating nucleotide is incorporated, thereby producing an extended primer; and

c) determining the mass of the extended primer, thereby determining whether a mutation is present in the target nucleic acid sequence.

29. The process of claim 28, wherein the chain terminating nucleotides are mass-matched.

30. The method of claim 28, wherein the mass of the extended primer is determined by mass spectrometry.

31. A process for detecting mutations in a plurality of target nucleic acid sequences in a sample, comprising:

a) hybridizing a plurality of primers to nucleic acid molecules in the sample, thereby producing a hybridized primers, wherein:

the nucleic molecules from the sample are optionally immobilized;

each primer is complementary to a sequence of a target nucleic acid sequence that is adjacent to a region suspected of containing a mutation sequence;

b) contacting the hybridized primers with a composition comprising a chain terminating nucleotide selected from a mass-matched dideoxyribonucleoside triphosphate or a 3'-deoxynucleoside triphosphate and one or more deoxyribonucleoside triphosphates, such that the hybridized primers are extended until a chain terminating nucleotide is incorporated, thereby producing an extended primer; and

c) determining the mass of the extended primers, thereby determining whether mutations are present in the target nucleic acid sequences.

32. The process of claim 31, wherein the chain terminating nucleotides are mass-matched.

33. The method of claim 31, wherein the mass of the extended primers are determined by mass spectrometry.

34. A method for detecting a target nucleic acid sequence, comprising the steps of:

a) hybridizing a primer to a nucleic acid molecule comprising a target nucleic acid sequence, wherein the primer can be extended in a 3' direction towards the target nucleic acid sequence, and wherein the 5' end of the primer can be selectively cleaved from the extension product;

b) extending the primer in the presence of mass matched deoxyribonucleotides and a polymerase to produce an extension product;

c) selectively cleaving the 5′ end of the primer from the extension product to produce a portion of the primer and a cleaved extension product; and

d) detecting the cleaved extension product.

35. The method of claim 34, wherein the cleaved extension product is detected by mass spectrometry.

36. A method for detecting a plurality target nucleic acid sequence, comprising the steps of:

a) hybridizing a primer or plurality thereof nucleic acid molecules comprising target nucleic acid sequences, wherein the primers can be extended in a 3′ direction towards the target nucleic acid sequence, and wherein the 5′ end of the hybridized mass-matched nucleic acid molecules can be selectively cleaved from the extension product;

b) extending the primers in the presence of mass matched deoxyribonucleotides and a polymerase to produce extension products;

c) selectively cleaving the 5′ end of the primers from the extension products to produce portions of the primers and cleaved extension products; and

d) detecting the cleaved extension products.

37. The method of claim 36, wherein the cleaved extension product is detected by mass spectrometry.

38. A method for detecting a target nucleic acid sequence, comprising the steps of:

a) hybridizing to a nucleic acid molecule comprising the target nucleic acid sequence

a first primer, which can be extended in a 3′ direction towards the target nucleic acid sequence, and wherein the 5′ end of the primer can be selectively cleaved from the extension product, and

a second primer, which can be extended in a 3′ direction towards the first primer;

b) extending the primers in the presence of mass-matched nucleotides to produce a double stranded amplification product;

c) selectively cleaving the 5′ end of the first primer in the amplification product, to produce a double stranded amplification product comprising a cleaved primer extension product comprising a 5′ portion and a 3′ portion;

d) denaturing the product of step c); and

e) detecting the 3′ portion of the cleaved primer extension product.

39. The method of claim 38, wherein the cleaved extension product is detected by mass spectrometry.by mass spectrometry.

40. A method for detecting a plurality target nucleic acid sequences, comprising:

a) hybridizing to each of a plurality of nucleic acid molecules comprising the target nucleic acid sequence

a first primer, which can be extended in a 3′ direction towards the target nucleic acid sequence, and wherein the 5′ end of the primer can be selectively cleaved from the extension product, and

a second primer, which can be extended in a 3′ direction towards the first primer;

b) extending the primers in the presence of mass-matched nucleotides or pair-matched nucleotides to produce double stranded amplification products;

c) selectively cleaving the 5′ end of each of the first primers in the amplification product, to produce double stranded amplification products comprising cleaved primer extension products comprising a 5′ portion and a 3′ portion;

d) denaturing the products of step c); and

e) detecting the 3′ portions of the cleaved primer extension products by virtue of the masses.

41. The method of claim 40, wherein detection is effected by mass spectrometry.

42. A method for detecting a target nucleic acid sequence, comprising

a) hybridizing first and second primers to a nucleic acid molecule containing the target nucleic acid sequence, wherein a primer contains a selectively cleavable site at its 3′ end;

b) extending the primers in the presence of mass-matched nucleotides;

c) cleaving the resulting product at the selectively cleavable sites;

d) analyzing the masses of the cleavage products, whereby the target sequence is detected.

43. The method of claim 42, wherein the cleaved extension product is detected by mass spectrometry.

44. The process of claim 43, wherein a plurality of primers are hybridized and a plurality of target sequences are identified in a single reaction.

45. The method of claim 44, wherein the cleaved extension products are detected by mass spectrometry.

46. A computer-based method for identifying nucleotide or nucleotides at one or more base positions in a target nucleic acid molecule or plurality thereof, comprising:

a) entering the primer sequence or primer mass, the mass of an individual mass-matched deoxyonucleotide into the computer and the identify of chain terminators used;

b) entering the masses of the fragments generated by a primer extension reaction, wherein the primer is extended by mass-matched deoxynucleotides;

c) determining P_{base}, wherein P_{base} is the base periodicity in daltons;

d) calculating $M_{diff}[n]$ for each nucleotide base to be identified, wherein:

$M_{diff}[n] = M_{obs}[n] - M_{PR}[n]$;

$M_{PR}[n] = (M_{primer} + M_{light}) + (n - 1) P_{base}$;

$M_{obs}[n]$ is the observed peak;

where:

n is the base position;

$M_{PR}[n]$ is the n^{th} periodic reference mass;

M_{primer} is the mass of the primer;

M_{light} is the mass of the lightest nucleotide terminator; and

e) determining the identity of a nucleotide at any base position or the positional mass difference by determining $M_{diff}[n]$ and comparing it to a database of previously calculated values of M_{diff} for each of the chain terminating nucleotides.

47. A system for high throughput analysis of nucleic acid samples, comprising:

a processing stations that performs a chain extension reaction, in the presence of mass-matched nucleic nucleotides, on a nucleic acid sample in a reaction mixture;

a robotic system that transports the resulting products from the processing station to a mass measuring station, wherein the masses of the products of the reaction are determined; and

a data analysis system that processes the data from the mass measuring station by performing the method of claim 46 to identify a nucleotide or nucleotides at one or more base positions in nucleic acid molecule in the sample.

48. The system of claim 47, further comprising a control system that determines when processing at each station is complete and, in response, moves the sample to the next test station, and continuously processes samples one after another until the control system receives a stop instruction.

49. The system of claim 46, wherein the mass measuring station is a mass spectrometer.